Overview of the Comité de l'Antibiogramme de la Société Française de Microbiologie

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The Comité de l'Antibiogramme de la Société Française de Microbiologie was founded in 1980 by Professor Yves A. Chabbert, who served as chairman for two years. The original members were: J. F. Acar, F. Bergogne-Berezin, R. Cluzel, A. Courtieu, P. Courvalin, J. Duval, C. Morel, A. Thabaut and M. Véron. The chairmanship was passed in 1981 to Professor Roger Cluzel, who chaired the committee until 1995. The membership was enlarged by approximately twenty to include microbiologists representative of both university-affiliated and non-affiliated hospitals, as well as a pharmacologist and a clinician.

Since its origin, the CA-SFM has held two annual meetings, and has met three times annually since 1992. In addition, working parties have at times solicited the collaboration of experts outside its membership for participation in a project on a given subject.

Until the present, the primary role of the CA-SFM has been to propose the breakpoints (concentrations and inhibition zone diameters) necessary for the determination of the susceptibility to new antibiotics. This has been carried out in several steps.

The first step consists in the establishment, prior to approval for marketing (AMM), of the provisional values for each antibiotic, including:

- the distribution of minimal inhibitory concentrations (MICs) of several thousands of bacterial strains, susceptible as well as with biochemically and genetically defined mechanisms of resistance, concerning antibiotics of the same class (evaluated in multicenter studies);
- the major pharmacokinetic parameters of the antibiotic, considered according to its different routes of administration.

This comparison of the microbiological and pharmacokinetic data permits the determination of the provisional critical drug concentrations used during the clinical trials of the product. The critical diameters are determined by using a plot of concordance or, in the case of a poor correlation, with the aid of a scattergram, which reduces to a minimum the major errors of interpretation. The antibiotic load of the disks is selected ahead of time; it is usually identical within a family of antibiotics (e.g. 5 μg for the fluoroquinolones).

The second step consists in the establishment of definitive breakpoints, taking into account the clinical results observed in the therapeutic data *agreed upon* by the AMM, and especially, the precise analysis of the documented clinical setbacks of bacteriologic origin.

Individual opinions on the criteria required for determining breakpoints to separate susceptible, intermediate and resistant categories were pooled, and in 1980 a formula was proposed. This formula, which includes different pharmacokinetic parameters, established a value for the weighted serum level available for the antibiotic which must be compared with the MIC histograms of the different bacterial subpopulations within a particular species. Ten years later the same type of formula was published by the BSAC. The importance accorded to the parameters involved varies from one country to another: intrinsic activity of an antibiotic against a particular bacterial species; pharmacokinetics and pharmacology related to doses and habitual routes of administration; and the biochemical and genetic data that characterize low- or high-level resistance of particular strains. This leads to corresponding differences from one country to another in the published susceptibility and resistance standards. The guiding principles of the CA-SFM were published under the title 'Definition and determination of *in vitro* antibiotic susceptibility breakpoints for bacteria in France' in the *European Journal of Clinical Microbiology and Infectious Diseases* in 1994. For this reason, low and high breakpoints separating susceptible–intermediate

and intermediate–resistant zones vary according to whether they are established by the National Committee for Clinical Laboratory Standards (NCCLS), by the BSAC or by the CA-SFM.

In certain cases, it was possible to consider a revision of these breakpoints for some products due to the appearance of a new mechanism of resistance or to a modification of the therapeutic data or the dosage prescribed, in conjunction with the pharmaceutical industry, which was involved as often as necessary for reviewing the data and reaching a consensus.

The CA-SFM also established a series of rules for the interpretation of the in vitro antibiotic susceptibility tests (the antibiogramme), taking into account an in-depth knowledge of the accepted mechanisms of resistance and of the technical procedures for their detection. These rules of interpretation most often concern the different members of one family of antibiotics for which the mechanism of resistance is the same. The important principles of the interpretative reading of the in vitro antibiotic susceptibility tests (the antibiogramme) were developed by P. Courvalin. They are based upon the precise analysis of the phenotype of resistance observed in vitro for a given strain; this analysis allows for the deduction of the accepted mechanism of resistance involved, and in this way, for the necessary adjustments. This is especially important in the case of a characteristic of resistance that is poorly expressed in vitro, where the use of a product involving this characteristic will manifest in a therapeutic setback. One of the most significant practical examples of this interpretative reading, described in detail by J. Sirot, concerns the detection of the strains that produce extended-spectrum β-lactamases by the disk method.

Since 1992, the CA-SFM has organized a working group for the purpose of revising the different techniques used for the determination of antibiotic sensitivity. This revision resulted in the precise recommendations that form the subject of one of the contributions to this supplement.

Additionally, the CA-SFM has taken the initiative, in conjunction with the Agence Française du Médicament, which is responsible for issuing the AMM, in establishing the antibacterial spectrum of the new antibiotics and in revising the oldest drug products and analyzing them by family.

The integration of the clinical results, the bacterial spectrum and the data provided by the surveillance of resistance for a particular antibiotic permits the establishment of the 'clinical spectrum' of this antibiotic. Thus, the bacterial species are divided into four classes: usually susceptible, moderately susceptible, resistant and non-constantly susceptible. The latter class provides epidemiologic information on the prevalence of the resistant strains. Before being definitively adopted, the clinical spectrum is submitted for consideration to the Syndicat National de l'Industrie Pharmaceutique or is discussed with representatives of the pharmaceutical industry.

The recommendations of the CA-SFM have been published since 1980 in a communiqué which is revised and updated annually. This communication is published in French and appears in the journal *Pathologie Biologie*, the *Bulletin of the Société Française de Microbiologie* and the *Bulletin of the Contrôle de Qualité* which is distributed to the analytic laboratories of medical biology. It is also distributed as part of the abstract publication for the annual meeting in Paris, the first week of December, entitled *Réunion Interdisciplinaire de Chimiothérapie Anti-Infectieuse* (RICAI). The 1996 version of this communication is included as part of this supplement.

Throughout the years, the CA-SFM has been invited to present its point of view at various international congresses, most recently at the European Congress of Clinical Microbiology and Infectious Diseases in 1989 and 1995, at the International Congress of Chemotherapy in 1993 and at the Biannual Conference on Anti-infective Drugs and Chemotherapy in 1994.

In the interests of international harmony, it is imperative that the CA-SFM reinforce its relations with the other national and international committees. This would allow for the dissemination of a 'pragmatic consensus' and the elimination of potentially discrepant interpretations of the same strain, resulting in epidemiologic studies of a consistently high quality.